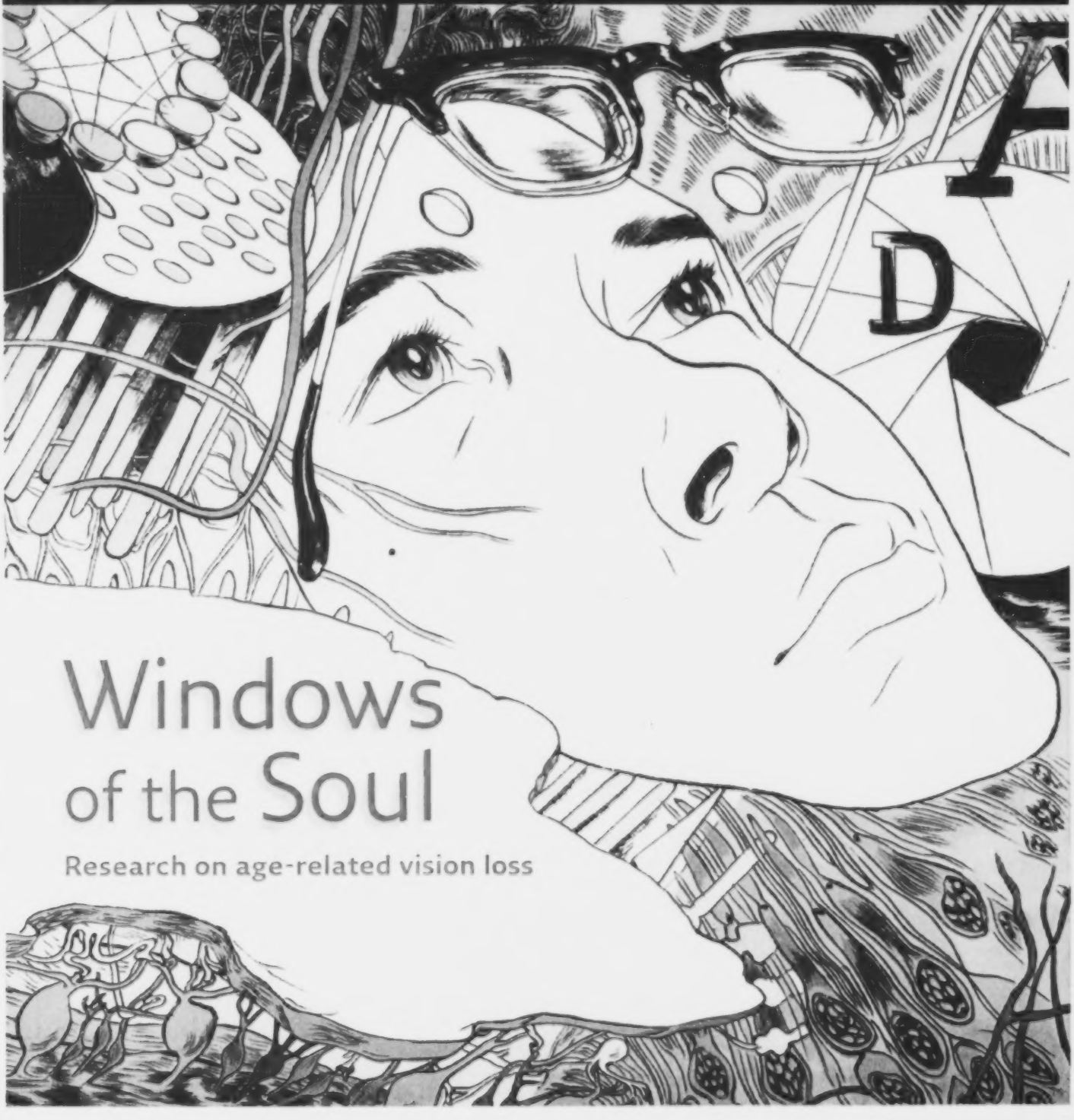
MEDICINE AND THE ARTS | INTESTINAL DISEASE | PHYSICAL ACTIVITY MESSAGES

Research News

ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH FALL 2007



Windows of the Soul

Research on age-related vision loss

On the cover

Jillian Tamaki was raised in Calgary where she graduated from the Alberta College of Art and Design. She now lives in Brooklyn, NY where her illustration clients include *The New Yorker*, *The New York Times*, CBC, and *Maclean's* magazine.

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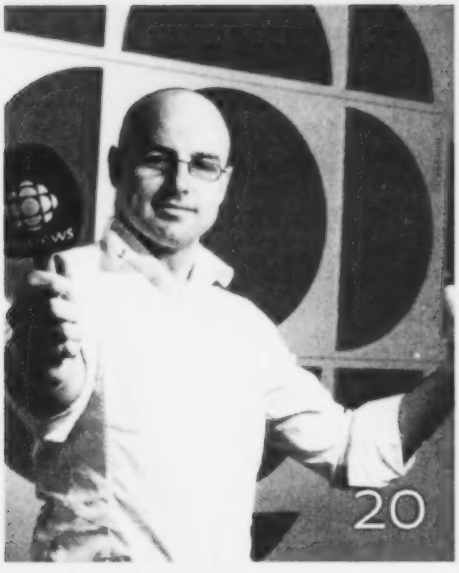

IN EVERY ISSUE

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An art and a science

A program at the University of Alberta seeks to balance the study of medicine with a healthy dose of the arts and humanities

"The practice of medicine is very closely intertwined with issues of governance, budgets, and social agendas, as well as issues of human drama, loss, and hope. . . I think it's a big mistake, and an incredibly huge loss, if doctors simply resign themselves to being technicians."

So says Vincent Lam, emergency physician and the 2006 winner of the prestigious Giller Prize for his book of short stories, *Bloodletting & Miraculous Cures*. If Dr. Lam's words summarize a problem with the practice of medicine, his very identity embodies part of its solution. As a doctor and a writer, he embraces both scientific and artistic elements. And if the practice of medicine is truly both a science and an art, as many claim, shouldn't all healthcare professionals be exposed to both aspects in their training?

In fact, more and more medical schools are trying to connect the area of overlap of the arts and humanities on the one hand, and health and medicine on the other—a domain often referred to as "the medical humanities". In Canada many medical faculties have incorporated some aspects of the medical humanities into their curricula, but a program at the University of Alberta, launched in May 2006, is only the second initiative in the country devoted solely to the medical humanities. According to its mission statement, this program aims to create a balance of science and the humanities within the Faculty of Medicine and Dentistry, in order to help develop "well-rounded health professionals who are skilled, caring, reflexive, and compassionate practitioners".

> The practice of medicine is both a science and an art

The Arts and Humanities in Health and Medicine Program (AHHM) was championed by Dr. Tom Marrie, who came to the University of Alberta from Dalhousie University, the home of Canada's very first medical-humanities program. Upon his appointment as dean of medicine and dentistry, he decided to establish a similar presence here. "It seemed to me that a program in the humanities would help our students in many ways," he explains. "Sensitization to human suffering and the element of reflection that is necessary in the humanities do make one a better doctor."

The program is co-directed by Dr. Verna Yiu, a pediatric nephrologist and the Faculty's assistant dean of student affairs, and Dr. Pamela Brett-MacLean, whose recently defended Ph.D. dissertation concerned aging, the arts, and well-being. The two proposed a broad program that would recognize current activities in areas often considered to be medical humanities—law, ethics, and history. But that's not all. The program may also encompass "multicultural and international health, care of the elderly, end-of-life care, human values, complementary and alternative medicine, and other areas in the arts and social sciences (e.g., religious studies, psychology)."

"We want to create connections with ongoing efforts, but also create new connections in different arts and humanities areas, and with different faculties and organizations," explains Dr. Brett-MacLean.

Since the curriculum for medical and dental students is already jam-packed, much of the arts and humanities program's offerings are extracurricular. To date, the program has collaborated to organize events such as a series of monthly speakers;

a visit and reading by Vincent Lam; an exhibition of the art of Robert Pope ("Reaching out with hope and healing"); a book launch (François Martin Mai's Diagnosing *Genius: The Life and Death of Beethoven)*; and a performance of *Ball*, a one-act play about a young man's experience with testicular cancer. Writing workshops have been popular, and this fall a "Writer-in-Medicine" position will be launched to provide feedback on writing submissions and share expertise with writing and publishing. An approach called narrative medicine—which encourages physicians and medical students to write about their patients in a way that goes beyond the bare facts of a medical chart, in order to help them better understand the person—is also being developed, starting with a reading group of medical students and doctors.

The AHHM program offers many opportunities to partner with other organizations in the community. An arts-and-science symposium will take place in November to help celebrate Edmonton's designation as the Cultural Capital of Canada for 2007. From January to May 2008 the program will also present a film festival entitled "Good Medicine" in partnership with the Edmonton Public Library.

> Medicine is a very human endeavour

At a time when health care is increasingly governed by the pressures of funding, sustainability, and technology, the Arts and Humanities in Health and Medicine Program reminds us that, at its root, the practice of medicine is still a very human endeavour.

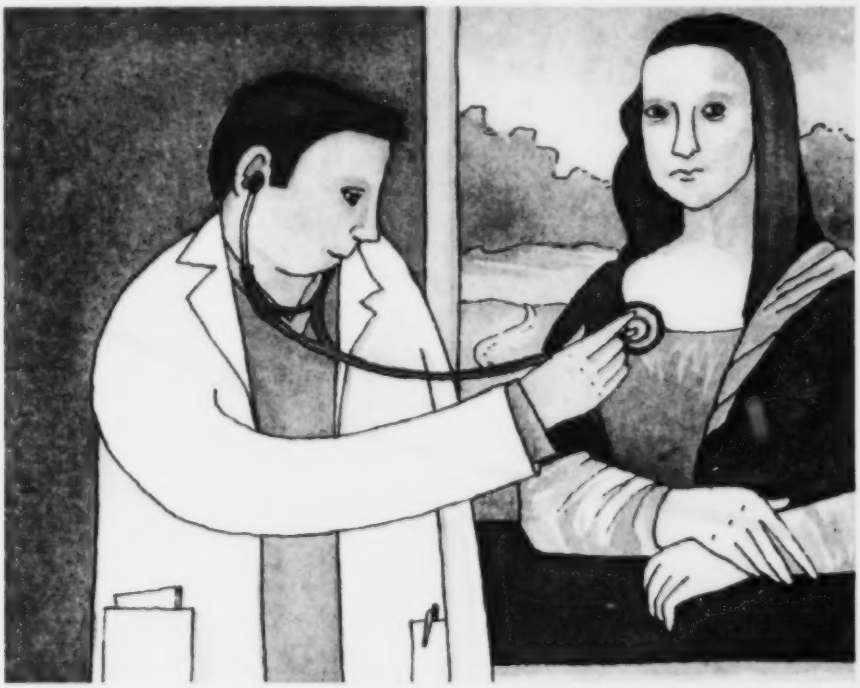
Recommended websites

University of Alberta Arts and Humanities in Health and Medicine Program

http://www.med.ualberta.ca/education/ahhm.cfm

Edmonton 2007 Cultural Capital of Canada: Symposia and Speakers Series

http://www.edmontonculturalcapital.com/symposiaspeakersseries.asp



Getting the message across

What makes us respond to certain messages about physical activity and not to others?

IT'S A WELL-KNOWN FACT THAT EXERCISE HAS CONSIDERABLE PHYSICAL BENEFITS. Despite this, many Canadians remain sedentary, putting themselves at risk for obesity, cardiovascular disease, type 2 diabetes, and cancer. AHFMR Population Health Investigator Dr. Tanya Berry wants to know how to get people to tune in and adopt more active lifestyles.

An avid runner and soccer player, Dr. Berry carries her passion for exercise into her research. "I'm really trying to improve the effectiveness of physical-activity messages. It seems like a simple question—'What is the best message to get people moving?'—but it's actually quite difficult to answer," she says. Something that makes one person pay attention to a message may not get another's attention. Similarly, what motivates one person to become active may not motivate someone else. It's like a jigsaw puzzle of questions: only when all the questions are answered can the big picture—and the best messages—become clear.

Picture this . . .

One key to solving the puzzle may lie in how people visualize symptoms. "Symptoms that can be better visualized may make for more effective messages," says Dr. Berry. By way of illustration, she cites high blood pressure, a condition known as "the silent killer" because of its lack of apparent symptoms. People readily associate a heart attack with symptoms such as pain in the arm or tightness in the chest, but they find it difficult to visualize what it is to have high blood pressure, which makes it difficult to design a message that communicates effectively the benefits of physical activity as a means of reducing risk.

But for whom are these messages effective? People in their fifties and sixties who are prime candidates for high blood-pressure and its consequences—including heart attacks—will likely find risk reduction good motivation to become more active. Twenty-somethings may be less affected by this type of health-promotion message; they may be more susceptible to glossy images of glamorous models as physical ideals.

Knowing the competition

"Health-promotion messages are a small part of the whole advertising world," explains Dr. Berry. "There are a million other messages floating around out there, and we really don't know what effects these messages are having. Furthermore, we don't know whether we can compete with these messages or whether we should simply coexist with them."

This is of particular concern with younger people, who may be motivated to be active for reasons of appearance rather than improved health. Dr. Berry wants to determine how different forms of exercise-related advertising influence people. "Perhaps we can use the advertising that's out there to turn young adults on to physical activity for health reasons too. That's what all this work is about: creating a fit, healthy adult population."

Dr. Berry carries her passion for exercise into her research

About the researcher

Dr. Tanya Berry is an *AHFMR Population Health Investigator*, an assistant professor in the Faculty of Physical Education and Recreation at the University of Alberta, and a research associate with the Alberta Centre for Active Living.

Selected publication

Berry TR. Who's even interested in the exercise message? Attentional bias for exercise and sedentary-lifestyle related words. *Journal of Sport and Exercise Psychology.* 2006 Mar;28(1):4-17.

Recommended websites

Alberta Centre for Active Living
http://www.centre4activeliving.ca

Fighting intestinal disease from within

In Canada, more than 200,000 lives are seriously affected by diseases of the bowel and colon. Unfortunately, we don't know what causes many of these debilitating and chronic diseases—let alone how to cure them.

COMPLAINTS RELATED TO THE STOMACH AND INTESTINES FEATURE AMONG THE TOP THREE REASONS PEOPLE GO TO SEE A DOCTOR. Attempts to address those gastrointestinal problems account for up to 15% of total direct healthcare spending in Canada—which is more than we spend on either cardiovascular or mental-health problems. So, given that over eight million Canadians suffer from gastrointestinal problems, finding out just how our intestines work could make a big difference to the healthcare system and our efforts to prevent disease.

AHFMR support helped bring Dr. Derek McKay to Alberta from McMaster University in 2006. Now a member of the Gastrointestinal Research Group at the University of Calgary, Dr. McKay heads a team of researchers working to understand the physiology of the small and large intestines (which include our bowels and colon).

In the fight against intestinal disease, their research concentrates on a trio of diseases affecting the lower abdomen that are not only painful, but often painfully embarrassing. Symptoms include abdominal pain, bloating, diarrhea, and constipation. Inflammatory bowel disease, a condition that severely reduces quality of life for about 200,000 people in Canada, actually comprises two different intestinal diseases: *Crohn's disease* and *ulcerative colitis*. Completing the trio is *irritable bowel syndrome*, the most common gastrointestinal diagnosis worldwide. In Canada it affects 13% to 20% of the population.

These numbers add up to a lot of suffering caused by a kind of disease that most patients don't want to talk about. In our intestine-shy culture it seems that the less said about bowel disease, the better. However, bowel disease is increasing in world populations. Dr. McKay notes, "It's vitally important to increase public awareness on the issue of bowel disease. There is so much unnecessary stigma attached to anything that goes wrong below the waist."

A parasitologist by training, Dr. McKay says that one of his favourite projects is the study of tapeworm parasites and their role in intestinal immune responses. Though using an actual tapeworm as a treatment may seem unpalatable to some and impractical to others, Dr. McKay hopes this research can help him find a way to mimic the desired immune responses that tapeworms can initiate—which block or reduce the severity of such intestinal disorders as irritable bowel disease.

Another exciting research project under Dr. McKay's guidance aims to determine how our intestines "know" when to let nutrients into the

bloodstream, while keeping bacteria and toxins out. Considering that a person's gut is essentially one long tube that has been divided into different structures—mouth, esophagus, stomach, and bowels—this barrier function must be extremely sophisticated. Dr. McKay's research in this field is specifically focused on the function of the mucous cells lining the internal surface of the intestine.

As a recognized leader in gastrointestinal research, Dr. McKay has ample knowledge to share with the world. He is the recipient of a prestigious 2007 Masters Award in Gastroenterology and holds a Canada Research Chair in Intestinal Immunophysiology in Health and Disease. Though only mid-career, Dr. McKay has already supervised 38 research trainees studying at undergraduate, master's, doctoral, and postdoctoral levels. His work includes an emphasis on working with student researchers for several reasons. "It's more fun having students around. Young people help keep labs vibrant," he admits. Moreover, students provide a crucial element of continuity in research. That continuity could be a key factor in eventually finding cures or even preventing diseases altogether.

> It's vitally important to increase public awareness on the issue of bowel disease

About the researcher

Dr. Derek McKay is an *AHFMR Scientist* and a full professor in the Department of Physiology and Biophysics in the Faculty of Medicine at the University of Calgary.

Selected publication

McKay DM, Watson JL, Wang A, Caldwell J, Prescott D, Ceponis PMJ, Di Leo V, Lu J. Phosphatidylinositol 3'-kinase is a critical mediator of interferon-γ-induced increases in enteric epithelial permeability. *Journal of Pharmacology and Experimental Therapeutics*. 2007 Mar;320(3):1013-1022.

Recommended websites

Canadian Association of Gastroenterology
http://www.cag-acg.org

Crohn's & Colitis Foundation of Canada
http://www.ccfc.ca

Age-related vision loss has been called North America's newest epidemic. As baby boomers age, vision loss is set to become an even bigger public-health issue. There are no cures, no ways to restore sight to those with age-related blindness as a result of such major conditions as diabetic retinopathy, age-related macular degeneration, and glaucoma.

Windows of the Soul

From the lab to the clinic

■ In a study entitled Vision Problems in the U.S., released in 2002 by the National Eye Institute, it was estimated that more than one million Americans aged 40 and over were blind, and an additional 2.4 million were visually impaired. These numbers were expected to double within 30 years as baby boomers move into old age. Canadian baby boomers are also developing eye diseases at alarming rates. Their chances of developing irreversible age-related blindness by age 75 is higher than 1 in 4.

The need for research is clear. Because genetics plays a role in most of the major eye diseases, ocular genetics has become an important tool in understanding these diseases. In the 1970s the University of Alberta established a specialization in ocular genetics that has been strengthened over the years as key researchers have been recruited.

One of the more recent recruits is Dr. Yves Sauvé, an electrophysiologist who joined the university in 2005. He studies the electrical properties of biological cells and tissues, and has a particular interest in using electrophysiological techniques to assess degeneration in the visual system and to devise appropriate therapies.

Age-related macular degeneration, the leading cause of blindness in the elderly of the Western world, is the main area of his research. Dr. Sauvé works with a model that closely mimics the disease—a mouse with a *mutation*. A mutation is a change in DNA sequencing; it can occur spontaneously in nature, or it can be brought about deliberately in the lab. Dr. Sauvé's model

Age-related macular degeneration is the main area of Dr. Sauvé's research

involves a particular gene that is linked with the production of polyunsaturated long-chain fatty acids. Working with the University of Alberta's Dr. Tom Clandinin, an international expert in the metabolism of fatty acids, Dr. Sauvé has begun small-scale trials with the mutated mice, enriching their food with a particular omega-3 fatty acid which is essential for vision. Results show that degeneration of the retina slows down. "We're very excited by the results, but this is very early going," notes Dr. Sauvé. "We don't yet understand how vision deteriorates in [these mutated] mice and how this deterioration might be delayed by dietary supplementation. We are not ready to translate this to humans—but our results to date are promising."

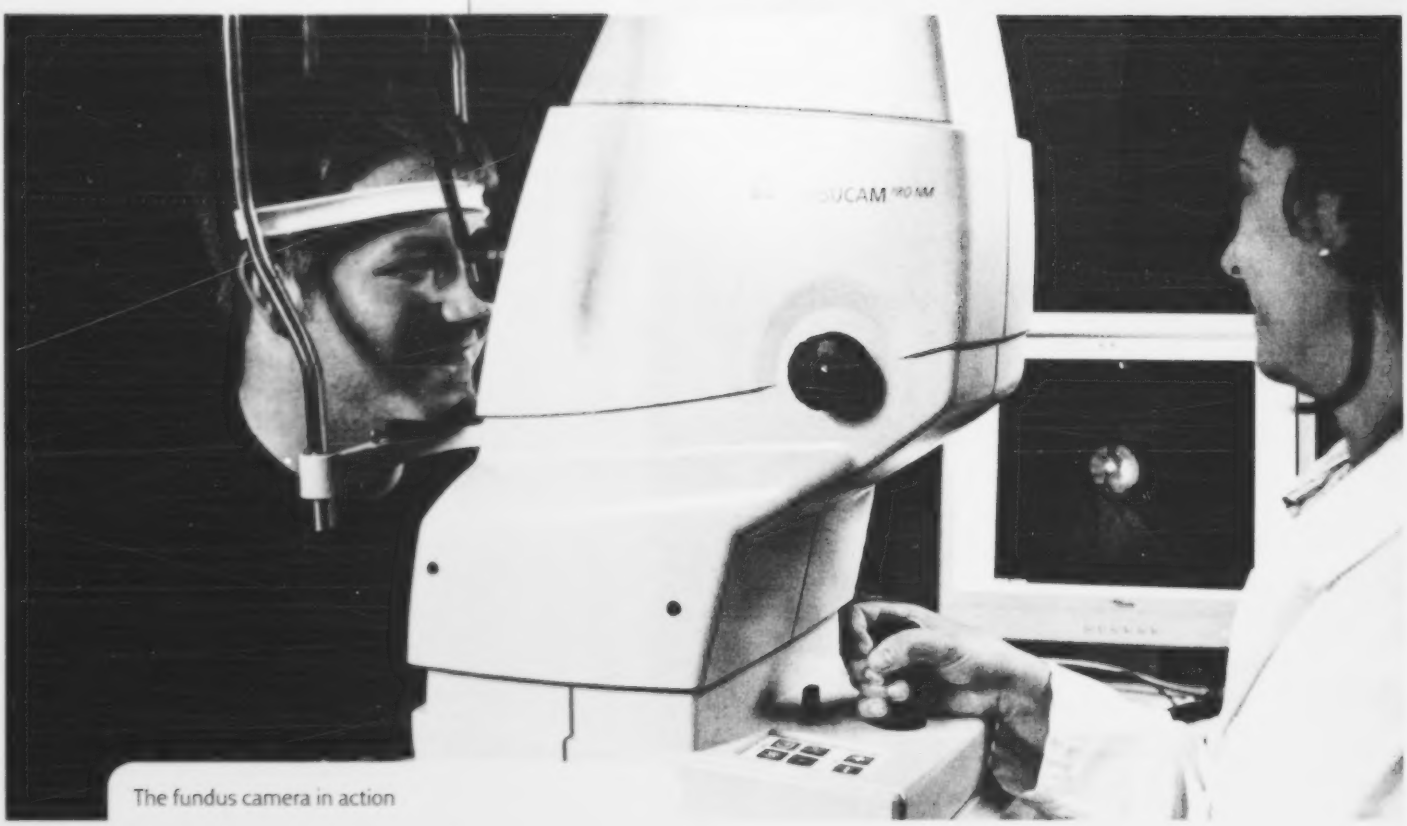
As part of this work, Dr. Sauvé's team is developing tests to detect early signs of vision loss in age-related macular degeneration. His main tool is the *electroretinogram*, which measures the response of the retina to light (See "Cool Tools", page X.). It can distinguish between the response of the *cones*, cone-shaped structures in the eye which function in bright light and detect colour, and the *rods*, which are used in night vision and peripheral vision. "When patients notice something wrong with their vision, it's usually rather late—when the cones have been affected," he explains. "We have preliminary evidence that there is a slight rod dysfunction before that, but it goes unnoticed. We think we may be able to pick up this problem using an electroretinogram.

People with macular degeneration may experience shadowy areas in their central vision

About the researcher
Dr. Yves Sauvé is an assistant professor in the departments of Physiology and Ophthalmology at the University of Alberta.

Selected publication
Alvarez BV, Gilmour GS, Mema SC, Martin BT, Shull GE, Casey JR, Sauvé Y. Blindness caused by deficiency in AE3 chloride/bicarbonate exchanger. *Public Library of Science ONE*. In press 2007.

Cool tools



The fundus camera in action

Looking deep into the eyes

Two key pieces of equipment dominate Dr. Yves Sauvé's laboratory at the University of Alberta. One is a fundus camera. This specialized low-power microscope has an attached camera that takes highly detailed photographs of the retina (the thin layer of cells at the back of the eye that responds to light). The camera in Dr. Sauvé's lab can take pictures of both animal and human eyes. He uses it to examine the anatomy of the retina.

But what the fundus camera can't do is assess function. "Just because the eye looks normal, that doesn't mean it is working correctly," says Dr. Sauvé. Take congenital stationary night blindness, for example. This is a condition in which people are born with a problem involving communication between nerve cells in the retina. The fundus camera would seldom find anything wrong with their eyes.

Enter the electroretinogram (ERG), which measures the response of the retina to a light stimulus. An electrode placed on the eye behind the lower eyelid records electrical activity. "The ERG is the central piece of my lab," says Dr. Sauvé. "This is a non-invasive test and can be used for animals and humans to detect very small dysfunctions in the rods [cells used for night vision] and cones [cells used for colour and daylight vision]. We can use the ERG to distinguish between problems with the rods and problems with the cones, as well as get insight as to how neural processing works in the retina. It's an amazing window into what is going on in the retina."

Dr. Yves Sauvé received an *AHFMR Major Equipment Grant* to purchase the fundus camera and ERG set-up.

Glaucoma

Another important eye disease is glaucoma, the leading cause of blindness worldwide. In glaucoma, fluid pressure inside the eyes slowly rises, damaging the *optic nerve*—the nerve that transmits visual information from the eye to the brain. There is no cure for the disease, but medications can lower eye pressure in glaucoma's early stages, thus slowing progression of the disease and helping to save vision. Glaucoma is inherited in about 50% of sufferers.

■ One of the world's leading glaucoma geneticists is Dr. Michael Walter. When he arrived at the University of Alberta in 1993, Dr. Walter began intensive research to identify the genes responsible for some severe types of childhood glaucoma. A major breakthrough in his lab was the identification and cloning of the *FOXC1* gene, a mutation of which causes one form of early-onset glaucoma.

"But identifying genes and knowing what mutations cause glaucoma doesn't tell you how or why glaucoma happens," says Dr. Walter. "That's why my research has shifted in recent years. I'm interested in understanding what certain genes normally do, what happens when they mutate in glaucoma, and what we can do to prevent damage to the optic nerve."

Dr. Walter's research centres on two genes that are both of a type called *transcription factors*: genes that regulate the functions of other genes. *FOXC1*, for example, probably affects about 2000 genes, not all of which are involved in glaucoma. When controller genes such as these mutate, their ability to regulate other genes is compromised—they might not activate a gene at the right time or to the right extent, or they might not turn it on at all.

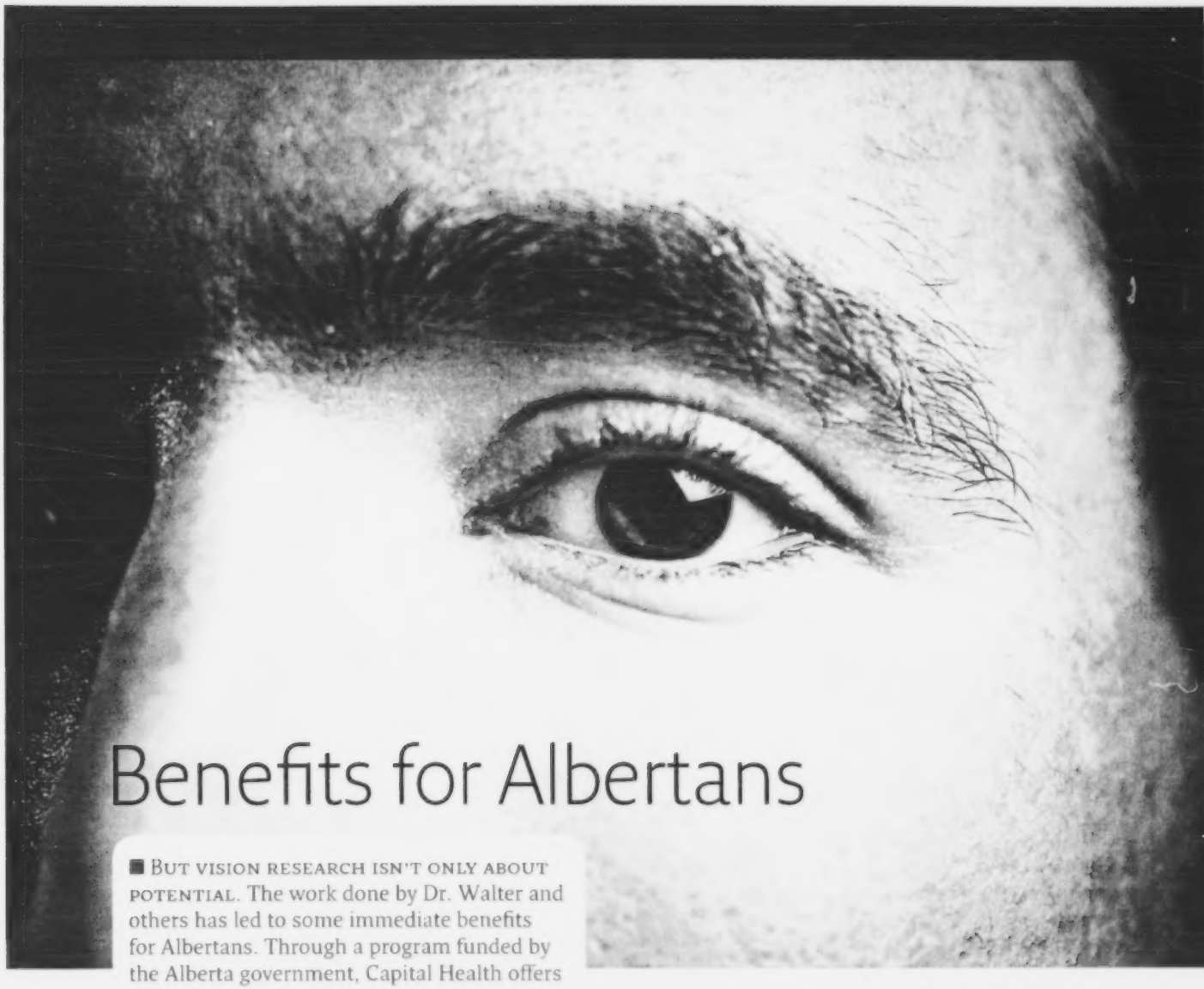
"It's a cascade effect," says Dr. Walter. "While this might sound complicated—and it is—these pathways also open up opportunities for therapy. We may not be able to fix the transcription factor, but we may be able to intervene at a downstream point and fix other genes in the pathway so that the end result is no disease. While we can't do this right now, it illustrates why understanding the pathways through which genes function is so important."

One of the world's leading glaucoma geneticists is Dr. Michael Walter

About the researcher
Dr. Michael Walter is a full professor in the Department of Medical Genetics, which he chairs, and the Department of Ophthalmology at the University of Alberta. He received AHFMR support for 10 years.

Selected publication

Walter MA. PITs and FOXes in ocular genetics: the Cogan Lecture. *Investigative Ophthalmology and Visual Science*. 2003 Apr;44(4):1402-1405.



Benefits for Albertans

■ BUT VISION RESEARCH ISN'T ONLY ABOUT POTENTIAL. The work done by Dr. Walter and others has led to some immediate benefits for Albertans. Through a program funded by the Alberta government, Capital Health offers molecular diagnostic testing to patients who may have inherited eye disorders. Currently the service is geared mainly to glaucoma. Patients with strong family histories of glaucoma can be tested to see whether they carry any of the mutations known to predispose people to the condition. If they do carry one of these mutations, frequent eye examinations are recommended, so that, if glaucoma was diagnosed in the future, they would be able to start treatment at an early stage. If they don't have the mutations, they are at no more risk than the rest of the general population and do not require frequent testing.

"To our knowledge this service, which is funded by the province, is unique in the world," says Heritage Clinical Investigator Dr. Ordan Lehmann, an ophthalmologist and genetics researcher at the University of Alberta. "We're translating basic research to improve the clinical service we offer patients. As we identify more genes that cause disease, they can be built into the testing process."

The close link between basic science and patient care is one of the things that attracted Dr. Lehmann to Alberta from the United Kingdom in 2004. "Every so often a patient comes along who sparks an important research question," he says. "As a clinician-scientist, I can take those questions and investigate them in the lab." For example, Dr. Lehmann was intrigued by a young patient referred to him with developmental eye disease. By studying her DNA, he and his lab colleagues were able to narrow the problem down to a particular gene that, when it mutates, causes

a number of eye diseases, including childhood blindness. The work was done in partnership with Dr. Andrew Waskiewicz, a professor of biological sciences who directs the University of Alberta zebrafish facility. The zebrafish is an important animal model for vision research.

The project highlights Dr. Lehmann's interest in chromosomal abnormalities—that is, extra copies of chromosomes, or missing chromosomes. For decades, these have been known to cause such relatively rare diseases as Down syndrome. "Besides that, it was assumed that chromosomes were relatively boring repositories of information that didn't do very much," explains Dr. Lehmann. In fact, nothing could be further from the truth. In the past few years, technology has improved to the point where it is possible to detect very small duplications and deletions in chromosomes. Such rearrangements are now considered to be as important a cause of human disease as mutations (DNA sequence changes).

Capital Health offers molecular diagnostic testing to patients who may have inherited eye disorders

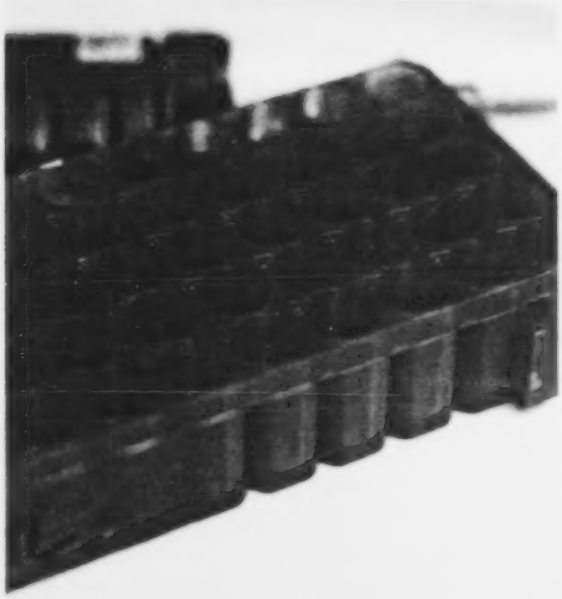
"My personal view is that real breakthroughs in vision science, as well as in other areas of medicine, are going to come from research at the molecular level," says Dr. Lehmann. "After all, some three-quarters of human diseases have a heritable basis. As a physician, I'm aware that knowledge about chromosomes and genes is not enough. The key challenge is to translate what you find into clinical practice. We're developing a team at the University of Alberta and Capital Health that is breaking down the barriers between the research lab and the clinic."

About the researcher

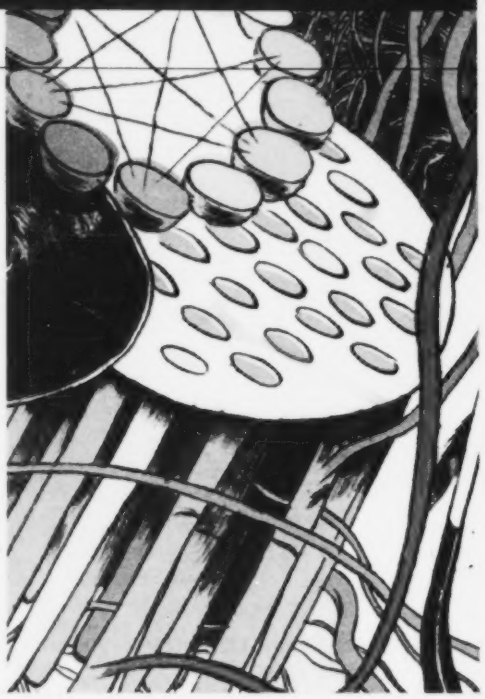
AHFMR Clinical Investigator **Dr. Ordan Lehmann** is an associate professor in the departments of Opthalmology and Medical Genetics at the University of Alberta.

Selected publication

Asai-Coakwell M, French CR, Berry KM, Ye M, Koss R, Somerville M, Mueller R, van Heyningen V, Waskiewicz AJ, Lehmann OJ. GDF6, a novel locus for a spectrum of ocular developmental anomalies. *American Journal of Human Genetics*. 2007 Feb;80(2):306-315.



Clues to treatment from the developing retina



When AHFMR Senior Scholar Dr. Sarah McFarlane was considering joining the University of Calgary, one of the things that impressed her most was the fact that senior researchers in neuroscience were still involved with laboratory work. She saw a dynamic group of scientists who were intent on adding new researchers and pushing research into new areas.

■ FAST-FORWARD TEN YEARS. Dr. McFarlane's instincts were on target. The University of Calgary has established itself as a leader in neuroscience: it is home to the Hotchkiss Brain Institute as well as numerous neuroscience-related research groups. Dr. McFarlane helped set up one of these—the Genes and Development Research Group—and now chairs it. Members examine genes that regulate developmental processes in all multicellular animals, from worms to humans.

One of Dr. McFarlane's research themes is the development of *neurons* (nerve cells) in the eye. While this is basic research, it has important links to human health because a number of diseases damage the optic nerve, which carries visual information from the eye to the brain. These include glaucoma; metabolic disorders such as diabetes, kidney failure, and thyroid disease; and fetal alcohol spectrum disorder. Diminished blood supply, with associated reduction in oxygen, to the optic nerve shortly before or after birth can also cause damage.

One potential strategy for fixing this damage could be to place stem cells into the adult nervous system and direct them to develop into ganglion cells in the *retina* (the light-sensitive tissue in the back of the eye). As they begin to grow, the ganglia develop filaments called *axons*, which then grow toward the visual centre of the brain.

Because none of this can be done currently, the big question is: How can you make it happen? As Dr. McFarlane notes, "We already have the answer: in the embryo. So if you could figure out how the retina develops in the embryo, it would give you clues about how to fix things in adults. That's what developmental neurobiologists like myself do. We try to figure out the molecules and mechanisms behind development. It's possible that what we reveal in our experiments will be the basis of future therapies."

Recently, Dr. McFarlane has been studying the process by which axons find their way to the appropriate destination—in the case of the retinal ganglion cells, the visual processing centre of the brain. How do they know how to get there? These axons have a structure at their growing tip called the *growth cone*, which interprets the

One of Dr. McFarlane's research themes is the development of nerve cells in the eye

chemical signals from molecules sent out by the message centre at their destination. Dr. McFarlane's lab has identified a number of the molecules that give out such signals.

"It's an enormous task to grow from the eye to the brain," says Dr. McFarlane. "We suspect that axons grow to a series of intermediate targets, where molecules tell them what to do, then go to the next intermediate target. We think that fibroblast growth factors, a family of proteins involved in development, control the chemical signals that tell axons to move on once they have arrived at an intermediate target. We're testing this idea now.

"The model system I work in is the frog. Its visual system develops in just three days, which makes it ideal. In the long term, I'd like to see the results from my work applied to mammalian systems, and eventually to people. But as a researcher, you can't do it all. Collaboration is key."

About the researcher
AHFMR Senior Scholar **Dr. Sarah McFarlane** is a full professor in the Department of Cell Biology and Anatomy at the University of Calgary.

Selected publication
Chen Y, Hehr CL, Atkinson-Leadbeater K, Hocking JC, McFarlane S. Targeting of retinal axons requires the metalloproteinase ADAM10. *Journal of Neuroscience*. 2007 Aug 1;27(31):8448-8456.

Recommended website
International Foundation for Optic Nerve Disease
http://www.ifond.org/

The genes in the developing retina

The potential for collaboration with Dr. McFarlane and other researchers in the field of neuroscience lured AHFMR Senior Scholar Dr. Carol Schuurmans to the University of Calgary in 2001. Her research centres on how neurons acquire their specific identities during development. One aspect of her work involves studying the genes that control the development of cells in the retina.

■ One of these genes is *Zac1*, a tumour-suppressing gene that has been studied extensively in cancer biology. Dr. Schuurmans did the experiments that first indicated the role that this gene plays in retinal development. Her team found that it limits the size

Dr. Schuurmans studies the genes that control the development of cells in the retina

Another of her research projects is done in collaboration with the Stem Cell Network, one of Canada's Networks of Centres of Excellence. Retinal stem cells could prove useful in cell-replacement treatments for degenerative diseases of the retina. Dr. Schuurmans works on identifying the genetic processes that result in turning stem cells into photoreceptors. Her team has already shown experimentally that retinal stem cells can be pushed toward this role. "But our efficiency is currently very low," notes Dr. Schuurmans. She hopes that by turning on various combinations of genes, photoreceptor differentiation can be boosted to levels that can be useful in treatment.

of the retina in the mouse by means of the processes of programmed cell death and the cessation of cell division. In the absence of the gene, retinal size is not properly controlled, so that the retinas of mice with *Zac1* mutations develop more cells than normal; in fact, they have not only extra cells but an extra layer of cells.

"Not a lot is known about how the retina becomes layered during development," says Dr. Schuurmans. "*Zac1* could be one of the first factors known that affects the migration of a specific population of retinal cells." Another intriguing finding is a related gene that works in opposition to *Zac1*, promoting rapid cell division in the retina. Dr. Schuurmans' goal is to further describe the functions of these two genes in the developing retina.

About the researcher *AHFMR Senior Scholar* **Dr. Carol Schuurmans** is an associate professor in the Department of Biochemistry and Molecular Biology at the University of Calgary.

Selected publication

Ma L, Cantrup R, Varrault A, Colak D, Klenin N, Götz M, McFarlane S, Journot L, Schuurmans C. *Zac1* functions through TG βII to negatively regulate cell number inthe developing retina. *Neural Development.* 2007 Jun 8;2:11.

Understanding retinal degeneration

To those who remark on the slow progress of science, Heritage Senior Scientist Dr. Paul Schnetkamp offers a reality check. He tells them about the *phototransduction cascade*, the process by which light is converted into electrical signals in specialized cells in the retina, called photoreceptors.

■ "When I started doing research in the late 1970s, we knew for sure about one protein involved in the *phototransduction cascade*. By the late 1980s, all major components of the cascade were known, with proteins identified and purified. The focus then shifted to retinal disease, where something goes wrong with phototransduction. Now 190 genes that cause retinal disease have been mapped, and 173 have been identified. Over the past six years, an average of 12 new retinal-disease genes have been mapped each year. The progress has been really quite amazing."

Understanding the genetics is important because mutations in genes are responsible for hereditary degenerative retinal diseases that cause blindness. Retinal degeneration affects more than 10 million North Americans. About 95% of these individuals have age-related macular degeneration, caused by an abnormal blood supply to the light-sensitive portion of the retina.

Dr. Schnetkamp studies a gene family by the name of *NCKX*, one of a small number of families that produce proteins necessary for phototransduction. The genes in this family make five proteins. Dr. Schnetkamp's research team discovered

Glossary

Structure in the eye

- **Rods** - so called because of their shape, these structures function in dim light and are used in peripheral vision
- **Cones** - cone-shaped structures which function in bright light and are adapted to detect colours.

one of them, one that is found only in the rod photoreceptors; they also study another one, which is found in the cone photoreceptors and throughout the brain.

Dr. Schnetkamp studies a gene family involved in phototransduction

All five of these proteins regulate the amount of calcium in cells. If they are not properly functioning, the rod or cone cells will not be able to get rid of calcium, phototransduction will stop, and vision will cease; too much calcium will eventually kill the cells. The key role these proteins play in the phototransduction process highlights the importance of this gene family in hereditary retinal diseases.

Dr. Schnetkamp has continued to study these proteins—cloning the genes, identifying their location on chromosomes, and screening patients with hereditary retinal disease to see if they have the mutations that could lead to blindness.

AHFMR has contributed approximately $10 million to vision-related research in Alberta since 1980.

"My focus has now shifted away from vision to trying to understand how these proteins actually work in the body," says Dr. Schnetkamp. "This detailed understanding is absolutely necessary. It's my belief that, with one or two exceptions, retinal disease is not going to be treated effectively by drug interventions. Gene therapy has been successful in several animal models of retinal degeneration. To apply this to retinal degeneration in human patients, we'll need to know which genes to target and how they function."

Interested in learning more about retinal degenerative diseases? The University of Calgary is hosting a conference designed for those suffering from these diseases, their families and friends, as well as vision care professionals. For more information go to **http://www.ffb.ca/visionquest/**

About the researcher
Heritage Scientist **Dr. Paul Schnetkamp** is a full professor in the Hotchkiss Brain Institute and the departments of Physiology & Biophysics and Biochemistry & Molecular Biology at the University of Calgary.

Selected publication

Kang K-J, Kinjo TG, Szerencsei RT, Schnetkamp PPM. Residues contributing to the Ca^{2+} and K^{-} binding pocket of the NCKX2 Na^{+}/Ca^{2+}-K^{+} exchanger. *Journal of Biological Chemistry.* 2005 Feb 25;280(8):6823-6833.

Recommended website

The Foundation Fighting Blindness (Canada)
http://www.ffb.ca/

Foundation Fighting Blindness (U.S.)
http://www.blindness.org/

From lab to newsroom

Students Jonathan Davies and Kristy Baron spent the summer working at CBC radio, thanks to AHFMR's Media Fellowship Program.

Kristy Baron

TYPICAL SUMMER EMPLOYMENT for most university science students involves running countless experiments in labs, battling the elements during field work, or staring at computer screens for hours every day.

This past summer, however, wasn't typical for Jonathan Davies, an M.Sc. student in the neuroscience program at the University of Calgary, or for Kristy Baron, a B.Sc. student in immunology and infection at the University of Alberta. Both traded in their lab coats for digital recorders and spiral notebooks—the basic tools of a journalist.

Davies and Baron were the 2007 recipients of the AHFMR Media Fellowship, which provides a stipend for two students to spend 12 weeks as reporters and researchers on science and medical stories at one of the province's major news organizations. Since 1991, when the program began, 29 students have been given this unique opportunity. Most of them have worked at CBC outlets. In the summer of 2007 Davies was posted at CBC Radio in Calgary, and Baron at CBC Radio in Edmonton.

They applied to the program for similar reasons: both saw a need for better explanation of scientific stories to the public. "When I got into science, I saw scientists who were doing fascinating work, but doing a lousy job of communicating

it," says Davies. "You can take the most interesting research in the world, and if scientists can't communicate it well, it's almost pointless."

Baron wanted to share her enthusiasm for scientific discovery. "When I think something *is cool, I want someone else to also think it's* cool—making people care about it, making them want to learn," she explains.

One of the goals of the Media Fellowship Program is to enhance the coverage of issues concerning science and technology by the media. Davies and Baron both used their specific scientific expertise to present their own weekly radio series—projects which likely wouldn't have been produced otherwise.

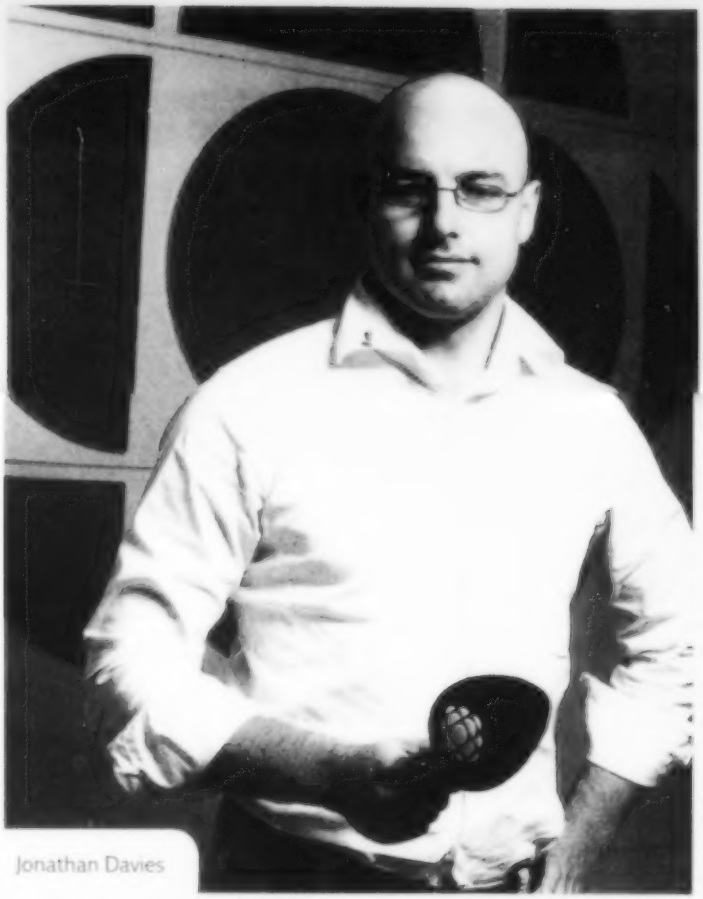
Baron's series was entitled *Microbes that live inside you and sometimes make you feel like crap.* Every week she interviewed a different professor about his or her research on a particular bacterium or virus. "I've always wanted to teach people about infectious diseases, and I got to be the person who set that up. That was a dream come true," Baron recalls.

In the series *Grey Matters: A look at the aging brain*, Davies also had the opportunity to develop an idea about which he is passionate. With so much attention focused on heart problems as people age, Davies felt it was time that more people knew about the changes their brains undergo, and ways of protecting their brains.

Joining busy newsrooms as novice journalists was certainly an exciting adventure for both students. There was all the radio jargon and technical skills to learn, as well as all the agony of waiting for prospective interview subjects who might or might not be available. But the most challenging aspects of the job didn't turn out to be the technical issues. Davies found that "the hardest thing is how to get a very complex idea across—very quickly, in very simple terms."

Joining busy newsrooms was an exciting adventure for both students

He was certainly put to the test when asked to prepare his own master's degree supervisor for an on-air interview about the physiology of chronic pain. "I was thinking, this pretty much makes or breaks my program. If I can't do this, if I can't communicate my own research—well, then I've failed." Davies didn't fail. In fact, he received a congratulatory call from the representative of a support group for sufferers from chronic pain, thanking him for the good work.



Jonathan Davies

Both Baron and Davies recognize the value of the new skills they have developed. Baron hopes to pursue a career in public health, where the ability to communicate clearly is paramount. Davies, who recently received an AHFMR Studentship to support his research, also acknowledges the benefit his science will derive from the media fellowship: "I'll know how to sell my ideas. I'll know how to communicate them effectively. I'll know how to maintain people's interest. That's only going to make my science stronger, and it's going to make me a more successful scientist."

Two alumnae of AHFMR's Media Fellowship Program now write for Research News: Tara Narwani, who wrote this story and the one on page 26; and Erin O'Connell, who wrote the stories on pages 4 and 24.

A new way of looking at things

Edmonton's MSD Corporation has developed a specialized contact lens to help correct a condition of the cornea, says Rikke Dootjes.

About ForeFront

AHFMR's ForeFront programs work to apply health research into innovative products and services that lead to improved health. For more information go to **http://www.ahfmr.ab.ca/forefront**

AFTER MORE THAN 40 YEARS IN THE OPTICAL INDUSTRY, Rikke Dootjes has done just about everything: He has worked for a big optical company, started his own business, created a partnership, dissolved the partnership, rekindled the partnership, and evolved his business in line with new technologies sweeping the contact-lens business. But now he's doing something entirely new—research.

With help from AHFMR's ForeFront Program, Dootjes and his team are developing a new type of contact lens. Most contact lenses sit directly on the *cornea*, the clear part of the eye which covers the iris and pupil and lets light into the eye, facilitating sight. The larger *msd Lens* is a scleral lens, which means it sits on the *sclera*, the white of the eye, and does not come in direct contact with the cornea.

Dootjes knows scleral lenses well. His company, Edmonton-based Viscon Corporation, manufactures contact lenses, primarily specialty lenses. About four years ago, Dootjes's partner, Bill Sturm, developed an innovative soft lens called the Epicon lens. "It was a fabulous lens," says Dootjes. "We tried to make it in a rigid lens, but it wasn't that comfortable. Bill came up with the idea of making the lens larger. That got us thinking about the scleral lens market."

Scleral lenses are prescribed for a number of reasons, including eye trauma from surgery or an accident. However, they are most commonly used for a condition called *keratoconus*, in which the cornea becomes thin and protrudes, causing distorted vision. The rigid scleral lens covers the irregularity of the cornea and functions as the new refractive surface of the eye, with a film of tears filling in the space between the back of the contact lens and the front of the eye. A soft lens wouldn't work, because it would drape over the front surface of the eyeball and take on the same irregular shape as the cornea. Because scleral lenses don't sit on the cornea, there's no discomfort for the wearer.

Currently, scleral lenses are custom-made by only a very small group of highly skilled practitioners located around the world. Patients requiring treatment usually have to travel great distances to be fitted for the lenses. The cost is very high, even prohibitive in some cases.

> Dootjes and his team are developing a new type of contact lens

That's where the *msd Lens* comes in. As a mini scleral lens with a diameter of only 15.8 millimetres, it is smaller than the standard 28-millimetre scleral lens. The lens is designed to be comfortable and easily fitted; it transmits oxygen very well, which also keeps the eye healthy. Although the design of the *msd Lens* is complex, Dootjes's team has developed software that allows it to be made easily by licensed contact-lens manufacturers. This will keep costs down and facilitate wide distribution of the lens.

Dootjes and Sturm set up a new company, MSD Corporation, to develop and market the *msd Lens*, but without any revenue, money for research and development was in short supply. That's when Dootjes turned to AHFMR's ForeFront Innovation Program. It funds medical technologies that demonstrate potential to improve health care and achieve commercial success. MSD is using ForeFront support to help cover patenting and marketing costs. "Going through the scrutiny of the ForeFront process in order to get funding was one of the best learning experiences I've ever had," says Dootjes. "The questions asked by the ForeFront committee challenged me to rethink a number of aspects of our business plan."

MSD Corporation is currently in negotiations to license the technology to the United States market. "Our first plan was to manufacture the lens ourselves, but we're pretty sure now that licensing is the way to go," adds Dootjes. The *msd Lens* will be officially launched in January 2008 at the Global Keratoconus Conference in Las Vegas. Dootjes and his team are already working on a second generation of the lens which has a unique tear-flow control feature. Every time the wearer blinks, tears (along with any debris) are pushed out of slots on the lens.

In the long term, the company's goal is to break into the general corrective-vision market. "The *msd Lens* has a number of advantages—vision is much sharper, the lens lets in more oxygen for a healthier eye, and it lasts longer than a soft lens. We think it could compete in the bigger market, and we're eager to try. But small steps first."

Making the grade

An AHFMR program offers top Grade 11 students like Anna Wu the opportunity to spend the summer in a university research lab.

WHEN WE THINK ABOUT WHAT GOES ON IN LABORATORIES, television crime shows that feature forensic investigators using scientific evidence may come to mind. Or we might imagine the stereotype of the introverted scientist, complete with pocket protector and taped glasses, nose buried in a textbook. But every summer, Grade 11 students from various high schools around the province have the opportunity to separate fact from fiction by spending their summer doing research.

The Heritage Youth Researcher Summer (HYRS) program, which was developed and funded by AHFMR, matches up exceptional students with exceptional university researchers. Grade 11 students with a minimum average of 85% compete for coveted positions in labs at the universities of Alberta, Calgary, and Lethbridge. From the pool of 150 applicants, 48 students were selected to be this year's HYRS participants.

Anna Wu was one such student. She spent her summer working in the lab of AHFMR Senior Scholar Dr. Babita Agrawal, an associate professor at the University of Alberta, where she learned a considerable amount about research and researchers.

> Every summer, Grade 11 students from around the province spend their summer doing research

Anna's summer project was part of a larger body of research in Dr. Agrawal's lab: research looking at how the immune system functions to help clear viral infections. "I took a harmless bacterium, *Caulobacter crescentus*, which has been modified to express a new gene. The protein encoded by this new gene has the ability to make stem cells turn into—or 'differentiate' into—specialized immune cells called dendritic cells. So we take the *Caulobacter* with the new gene and add it to stem cells. If they become dendritic cells, then we have a new tool for research as well as therapy."

> Anna's summer project was part of a larger body of research

This repertoire of technical abilities sounds very impressive, but Anna says she has learned more than laboratory skills. "I think one of the most important things I've learned is how much time goes into research. You have to grow the *Caulobacter*—and that takes a while—and then watching the stem cells to see if they differentiate also takes time. If you mess up a step, you lose time; so you have to be really careful. I think that the people that do this work have to love it, because it can be difficult."

Dr. Agrawal has participated in the HYRS program in previous years, and she says that not only do the high school students learn in the lab, but they play another important role. "Many of the graduate students in my lab want to go on to be professors and run their own labs, and if you run your own lab you have to supervise students," she says. "These graduate students are mentors to the HYRS students: they show them how research is done and inspire them to want to do research. It's a wonderful experience for all."

Of course it's not all work; there is some play involved too. HYRS organizers also arrange evening outings. The students can take part in movie nights and minigolf tournaments and get to know the other high-school students participating in the program. Many become good friends. Anna says she also had fun with the people in Dr. Agrawal's lab. "Before getting involved with HYRS, I thought that researchers were geeks," she admits. "But everyone in Dr. Agrawal's lab is so outgoing and fun. We did a lot of stuff together."

Another research stereotype bites the dust.

About the researchers

Anna Wu is now a Grade 12 student at Ross Sheppard High School in Edmonton.

Dr. Babita Agrawal is an *AHFMR Senior Scholar* and an associate professor in the Department of Surgery in the University of Alberta Faculty of Medicine and Dentistry.

AHFMR funding partners

The Alberta Heritage Foundation for Medical Research (AHFMR) has contributed more than $900 million to Alberta's health-research community. The Foundation also relies on the contributions of many partners in building and sustaining health research in this province. To mention just a few, these partners include

- the Government of Alberta and its related ministries and programs;
- federal granting agencies such as the Canadian Institutes of Health Research, the Canada Foundation for Innovation, and the Canadian Health Services Research Foundation;
- international funding partners like the Wellcome Trust and the National Institutes of Health; and
- non-profit and voluntary funding agencies such as NeuroScience Canada, the Heart and Stroke Foundation, the Canadian Diabetes Association, and the National Cancer Institute of Canada.

Following **up**

Research News checks in with a researcher who has been exploring obesity rates in aboriginal communities.

IN RECENT YEARS, NEWS STORIES HAVE BEEN SOUNDING THE ALARM over a growing epidemic of childhood obesity among North American children.

Couch-potato lifestyles and high-fat, high-sugar diets are repeatedly blamed.

Disturbingly, in certain Cree populations of northern Quebec, rates of childhood obesity have been observed that are significantly higher than average. But are the same factors driving this problem?

AHFMR Population Health Investigator Dr. Noreen Willows explored this question in the summer of 2003. Using a community-based approach, she interviewed elders, members of band councils, local physicians, and public-health officers in three Cree communities in northern Quebec.

A major theme among elders was that today's children have so few opportunities to experience Cree traditional life. "They talk about the health-promoting aspects of living in the bush," Dr. Willows recounts. "It promoted physical activity."

Another theme was that the children are eating high-fat food that has low nutritional value. The elders frequently mentioned that traditional Cree foods were essential for health. By not eating those foods, they feel that their children's health has been jeopardized.

While the pragmatic elders knew that a complete return to a traditional Cree lifestyle was impossible, they clearly identified a number of factors within the communities that, by promoting a more traditional lifestyle, could play a role in reversing the trend toward obesity. "Because of the relative isolation of the communities in northern Quebec, children learn Cree first. It's spoken at home and they're aware that language unites them as a people," says Dr. Willows. Children also participate in bush camps, such as the spring goose break, where they're taught to hunt migrating geese.

In the near future, Dr. Willows hopes to begin the next phase of her research—developing culturally appropriate ways to reduce obesity rates in Cree children. But first she wants to finish her analysis of the rich body of interview material she has gathered. "I hope it will lend a more sophisticated understanding of health issues in Aboriginal communities, and will de-stigmatize some of these problems by showing how complex and how rooted in history they are. It will give them a voice."

About the researcher

AHFMR Population Health Investigator **Dr. Noreen Willows** is an assistant professor in the Department of Agricultural, Food and Nutritional Science at the University of Alberta. She also received support from the ***Health Research Fund***, administered by AHFMR on behalf of Alberta Health and Wellness.

Selected publication

Willows N, Johnson M, Ball G. Prevalence estimates of pediatric overweight and obesity in First Nations preschool children using international and U.S. reference criteria. *American Journal of Public Health*. Feb 2007;97(2):311-315.

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